REMARKS

The present application is directed to modified viral particles. Prior to this Amendment and Response, Claims 1-2, 28-31, and 33-47 were pending. In the present Amendment and Response to Restriction Requirement, applicants amend Claims 1-2, 34, and 39 and add new Claims 48-51. The amendments do not introduce any new matter. Support for the new claims is found, for example, in the specification on p. 20, lines 21-22, p. 27, lines 6-15, and on p. 52, line 27 through p. 53, line 19. Upon entry of the present amendment, Claims 1-2, 28-31, and 33-51 will be pending.

Interview

Applicants wish to thank Examiner Chen (hereinafter "the Examiner") for extending the courtesy of a personal interview on December 21, 2005. Applicants agree with the Interview Summary provided by the Examiner.

Claim Objections

The Examiner objects to Claim 34 for improper grammar. Applicants amend Claim 34 to recite "one or more proteins." Applicants assert that the amendment overcomes the objection and request that the objection be withdrawn.

Claim Rejections under 35 U.S.C. 112, Second Paragraph

The Examiner rejects dependent Claims 39 and 40, asserting that they lack antecedent basis with respect to the base claim. Applicants amend Claim 39 to depend on Claim 38 and assert that the amendment overcomes the rejection. Applicants request withdrawal of the rejection.

Claim Rejections under 35 U.S.C. 112, First Paragraph

The Examiner rejects Claims 2, 28-31, 37, 39 and 40 asserting that they fail to comply with the enablement requirement. The claims are drawn to partially delipidated

immunodeficiency viral particles that incite a positive immune response and protection against an infectious organism. The Examiner asserts that the claims are not enabled with respect to partially delipidated particles that protect from HIV infection. The Examiner states on p. 7 of the Office Action that the **compositions comprising particles for inducing an immune response are enabled**. Applicants amend Claim 1 to delete the term "protection." Applicants assert that the amendment overcomes the rejection of dependent Claims 2, 28-31, 37, 39 and 40. Applicants request withdrawal of the rejection.

Claim Rejections under 102(b)

The Examiner rejects Claims 1, 2, 28-31 and 33-47 under 35 U.S.C. §102(b) as anticipated by U.S. Patent No. 5,419,759 to *Naficy* (hereinafter "*Naficy*"). *Naficy* describes a method and device for treatment of HIV infection by removing blood from a patient and treating blood with organic solvents in a device for the purpose of killing the virus and the infected cells. Applicants respectfully traverse the rejection.

Applicants assert that *Naficy* fails to teach the partially delipidated particles recited in Claim 1 and fails to inherently anticipate applicants' claimed invention. Claim 1 recites a partially delipidated viral particle that initiates a positive immune response in an animal or human and comprises at least one exposed epitope not usually presented to the immune system of the animal or the human by a non-delipidated viral particle. *Naficy* fails to teach immunogenic viral particles that comprise exposed epitopes not usually presented to the immune system by a non-delipidated viral particle.

Naficy teaches a method and device for treatment of HIV infection by treating blood with organic solvents in an extracorporeal device **with the purpose of killing HIV virus and blood cells infected with HIV**. *See*, for example, *Naficy*, Abstract. *Naficy* teaches a method of reducing levels of HIV in patients' blood by killing the cell-free virus and stopping or substantially reducing the replication of the virus inside the infected cells. To this end, *Naficy* teaches a method of dissolving or destroying the lipid envelope, thereby destroying the glycoprotein spikes that are associated with the lipid envelope, which renders

the virus unable to penetrate and infect the healthy cells. *See*, for example, *Naficy*, Abstract, Column 6, line 12, Column 7, lines 41, 44, 53 and 64-68, Column 8, lines 1-2 and 43-45, Column 9 lines 58-60, Column 11, lines 14-15 and 24, Column 13, lines 33-34, Column 14, Claim 1, lines 34-40, Column 16, and Claim 15, lines 20-27. *Naficy*'s method begins by delipidating plasma containing cell-free virus and cells infected with virus, followed by returning plasma containing the killed cells to the patient. See, for example, *Naficy*, Column 10, lines 10-19. Applicants assert that returning the killed cells could be toxic to the patient. Only after the delipidation has killed the infected blood cells in the treated plasma, *Naficy* suggests separating the blood cells from plasma before delipidation. *See Naficy*, Column 13, lines 56-61. In contrast, applicants' method involves separating both red and blood cells from plasma prior to plasma delipidation. See, for example, the specification, p. 29, lines 4-14. *Naficy* fails to teach, suggest, or provide motivation to test immunogenicity of its delipidated plasma.

As discussed above, *Naficy* teaches destruction of the lipid envelope of the HIV virus and destruction of the glycoprotein spikes. Applicants assert that the method disclosed in *Naficy* at least **does not necessarily generate** immunogenic partially delipidated viral particles by exposing epitopes through partial delipidation. *Naficy's* method does not necessarily generate applicants' claimed immunogenic partially delipidated viral particles at least because *Naficy* uses the solvent treatment conditions under which all of the viral particles may be destroyed. Applicants submit herewith to the Examiner's attention the Declaration by Mr. Akeefe, which shows, in Exhibit C, electron micrographs demonstrating viral particles partially delipidated using 1% and 2% solvent. **These electron micrographs show that the viral envelopes are destroyed upon treatment with 5% solvent.** ***Naficy*** **teaches delipidation using solvent concentration of 5% and higher**. *See Naficy*, Column 9, lines 1, 10, 24, 26, 34, 38, 41 and 43.

In contrast, applicants disclose in Example 3, p. 52, line 27 through p. 53, line 19, delipidation of an immunodeficiency virus by mixing a simian immunodeficiency virus (SIV) solution with 10% diisopropyl ether (DIPE) in 10:1 ratio, resulting in **final DIPE**

concentration of <1%. Applicants assert that the delipidation conditions that they used resulted in partially delipidated immunogenic viral particles and did not lead to destruction of viral envelopes. In support, applicants offer Exhibit C in the Declaration by Mr. Akeefe, which provides electron micrographs demonstrating partially delipidated viral particles obtained by delipidation with 1% or 2% solvent. **These electron micrographs show that a significant proportion of the viral envelopes are present following delipidation with 1% or 2% solvent.** Thus, the partial delipidation method used by applicants resulted in partially delipidated particles comprising viral envelopes, including envelope proteins. In contrast, 5% solvent destroys viral envelopes and obliterates envelope protein epitopes from viral particles. *Naficy* teaches use of 5% or greater solvent concentration. Therefore, *Naficy*'s delipidation conditions do not necessarily result in the claimed partially delipidated viral particles.

Applicants present new Claims 48-50. New Claim 48 recites delipidation with 0.5% to 2.5% solvent. New Claim 49 recites the limitation "wherein the at least one exposed epitope is an envelope protein epitope." New Claim 50 recites the limitation "wherein the modified viral particle has a lower lipid content in an envelope." Support for these new claims is found, for example, in the specification on p. 20, lines 21-22, p. 27, lines 6-15 and on p. 52, line 27 through p. 53, line 19.

Delipidation under the conditions taught in *Naficy* does not necessarily result in the claimed partially delipidated viral particles. *Naficy* teaches 5% delipidation at room temperature for 5 minutes, but offers few other details on the delipidation conditions. For example, in Column 9, lines 1-16, *Naficy* teaches delipidation with 5-50% diethyl ether (by volume) for 5 or 10 minutes at room temperature, but fails to teach any mixing of solvent and plasma. In Column 9, lines 20-30, *Naficy* teaches delipidation with 5-20% diethyl ether for 5 or 10 minutes at room temperature but again fails to teach any mixing of solvent and plasma. In Column 10, lines 13-16, in a prophetic example, *Naficy* teaches delipidation by 10% ether or higher with agitation at room temperature, without offering details as to the agitation conditions or duration. The effect of the delipidation process depends on multiple

parameters. Under the conditions that *Naficy* teaches, delipidation probably leads to destruction of viral envelopes and, as a result, to destruction of viral particles. Accordingly the conditions taught in *Naficy* may fail to produce immunogenic viral particles recited in the claims.

In view of the foregoing and based on the current case law, *Naficy* fails to inherently anticipate applicants' claimed compositions. *See In re Robertson*, 169 F.3d 743, 745 (Fed. Cir. 1999) (in order for a reference to anticipate inherently, extrinsic evidence must clearly show necessary presence of missing descriptive matter). *Naficy* fails to teach the conditions necessary to generate viral particles upon delipidation with 5% solvent, such as mixing conditions, and therefore fails to anticipate the claims inherently. *See also In re Rijckaert*, 9 F.3d 1531, 1534 (Fed. Cir. 1993) (inherency not inevitable, but rather result of optimized conditions). In *Rijckaert*, it was held that assuming the variables giving rise to the claimed result was not sufficient to make the claimed invention inherently anticipated. *Id.* at 1533-34. Since one of ordinary skill in the art would have to optimize the conditions that *Naficy* fails to teach, such as mixing conditions, in order to avoid destruction of viral particles upon delipidation with 5% solvent as shown in the electron micrographs (Exhibit C), the teaching of *Naficy* is not sufficient to inherently anticipate the claimed composition. Both *Robertson* and *Rijckaert* are cited in MPEP 2112. Thus, under *Robertson, Rijckaert* and MPEP 2112, *Naficy* fails to inherently anticipate Claims 1, 2, 28-31 and 33-47.

Moreover, *Naficy* teaches the disappearance or elimination of viral infectivity upon delipidation, which shows that the delipidation conditions used in *Naficy* destroyed viral particles. *Naficy* teaches **no recovery of infectivity of "up to 7 logs of virus"** after incubation with 5% diethyl ether at room temperature for 5 minutes. *See Naficy*, Column 9, lines 10-11, 15-17, and 33-35. In contrast, applicants method results in **a 2.5 log reduction in infectivity of immunodeficiency virus upon delipidation, with the remaining virus titer of $10^{4.5}$**. *See* specification, p. 53, lines 16-17. Applicants present herewith new Claim 51 supported by the specification as indicated and reciting less than 2.5 log reduction in infectivity of partially delipidated particles. The delipidation of immunodeficiency virus by

applicants' method results in a reduction of infectivity as opposed to a complete elimination of infectivity. *Naficy* teaches disappearance of viral infectivity, indicating destruction of integrity of viral particles.

Applicants assert that the complete disappearance of infectivity taught in *Naficy* indicates that, upon delipidation, integrity of viral particles in *Naficy* was destroyed. **Upon delipidation, the plasma in *Naficy* would not contain immunogenic, partially delipidated viral particles**, as claimed in the present application, and shown in the electron micrographs. Delipidation using 5% solvent or above, as taught in *Naficy,* resulted in destruction of integrity of viral particles as shown in the provided electron micrographs. Therefore, for at least these reasons, *Naficy* does not inherently anticipate applicants' claimed composition. In support of the foregoing, applicants offer the Declaration by Mr. Akeefe submitted herewith. Accordingly, *Naficy* fails to teach the delipidation conditions for obtaining applicants' claimed partially delipidated, immunogenic viral particles and fails to inherently anticipate the claims.

In view of the foregoing, applicants assert that *Naficy* fails to anticipate Claims 1, 2 and their dependent claims. Applicants request that the rejection of claims under 35 U.S.C. §102(b) be withdrawn.

CONCLUSION

The foregoing is submitted as a full and complete response to the Final Office Action mailed September 26, 2005.

No additional fees are believed due, however, the Commissioner is hereby authorized to charge any deficiencies which may be required or credit any overpayment to Deposit Account Number 11-0855.

Applicants assert that the claims are in condition for allowance and respectfully request that the application be passed to issuance. If the Examiner believes that any informalities remain in the case that may be corrected by Examiner's amendment, or that there are any other issues which can be resolved by a telephone interview, a telephone call to the undersigned agent at (404) 815-6102 or to Dr. John McDonald at (404) 745-2470 is respectfully solicited.

Respectfully submitted,

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